

ABSTRACT OF THE INVENTION

Framework (FR) –patching is a novel approach to modify immunoglobulin for
5 reducing potential immunogenicity without significant alterations in
specificity and affinity. Unlike previous described methods of humanization,
which graft CDRs from a donor onto the frameworks of a single acceptor
immunoglobulin, we patch segments of framework (FR1, FR2, FR3, and
FR4), or FRs, to replace the corresponding FRs of the parent immunoglobulin.
10 Free assortment of these FRs from different immunoglobulins and from
different species can be mixed and matched into forming the final
immunoglobulin chain. A set of criteria in the choice of these FRs to
minimize or eliminate the need to reintroduce framework amino acids from
the parent immunoglobulin for patching is described. The approach gives
15 greater flexibility in the choice of framework sequences, minimizes the need
to include parent framework amino acids, and, most importantly, reduces the
chances of creating new T- and B-cell epitopes in the resultant
immunoglobulin.